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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/060,208	02/01/2002	Wilson Burgess	CI-0026	7581

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EXAMINER

MCKANE, ELIZABETH L

ART UNIT	PAPER NUMBER
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1744

DATE MAILED: 06/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/060,208

Applicant(s)

BURGESS ET AL.

Examiner

Leigh McKane

Art Unit

1744

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 February 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 107, 124-142, 149-154, 156-159, 165-167 and 169 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 107 is/are allowed.
- 6) ☒ Claim(s) 124-142, 149-154, 157-159, 165-167 and 169 is/are rejected.
- 7) ☒ Claim(s) 156 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 124, 125, 128-133, 137-142, 149, 157-159, 166, 167, and 169 are rejected under 35 U.S.C. 103(a) as being unpatentable over Freistedt et al (Abstract of DD 280466) in view of Horowitz et al (U.S. Patent No. 5,712,086).

With respect to claims 124, 125, 128, 129, 130, 137, 142, 159, 166, 167, and 169, Freistedt et al teaches a method for sterilizing soft tissue (brain) wherein the tissue is contacted with propylene glycol and a polyol, such as DMSO, glycol, pentitol, etc., frozen, and irradiated. See Abstract. Freistedt et al is silent with respect to using a third stabilizer and to the radiation being gamma radiation particularly.

Horowitz et al discloses a similar method wherein a biological material is contacted with a stabilizer and sterilized with a suitable dose of gamma radiation (1-40 kGy). See col.6, lines 48-65. As Peterson evidences that stabilized biological materials can be safely sterilized using gamma radiation, it would have been obvious to one of ordinary skill in the art to employ gamma radiation as the radiation source in the method of Freistedt et al. Horowitz et al further teaches the known use of multiple stabilizers, such as mannitol and tocopherol (Figure 4), to protect the tissue during irradiation. As both Freistedt et al and Horowitz et al evidence the use of at least *two* stabilizers, the addition of a third stabilizer is deemed obvious where there are no unexpected results.

As to claim 130, it is deemed obvious to employ the method of Freistedt et al to sterilize combinations of soft tissue (dural tissue) with hard tissue (such as bone), as one would have had an expectation of success when applying the method of Freistedt et al to other types/combinations of tissues.

With respect to claims 132 and 133, Freistedt et al teaches irradiating the tissue while frozen. As known in the art, frozen tissue has fewer free radicals as any water remaining in the tissue is immobilized. Thus, it is deemed obvious to maintain the tissue as cold as necessary to achieve the desired reduction in free radicals.

As to claims 138 and 139, the combination of Freistedt et al with Horowitz et al discloses a dose of 40 kGy. Regardless, it is deemed within the purview of one in the art to optimize total dose, as a result effective variable.

With respect to claims 140 and 141, as Freistedt et al discloses employing a 5-95% solution of the radio-protectant, it is deemed obvious to optimize the concentration/molecular weight used.

As to claim 149, Freistedt et al is silent with respect to maintaining the pH during irradiation. Horowitz et al, however, discloses that the pH of the tissue is maintained during irradiation (col.7, lines 43-45). In order to preserve the viability of the biological tissue, it is deemed obvious to maintain it at a suitable value during irradiation.

With respect to claims 157 and 158, Freistedt et al fails to disclose adding a sensitizer to the biological material before irradiation. Horowitz et al teaches sterilizing biological material wherein a sensitizer (purpurins, phthalocyanines, psoralens, etc.) may be added before irradiation. See col.6, line 64 to col.7, line 10. Horowitz et al discloses that the use of a sensitizer achieves preferential damage to the virus, but not to the

Art Unit: 1744

biological material. For this reason, it would have been obvious to add a sensitizer in the method of Freistedt et al.

3. Claims 126, 127, 134, 135, and 150-154 are rejected under 35 U.S.C. 103(a) as being unpatentable over Freistedt et al in view of Horowitz et al as applied to claim 125 above, and further in view of Peterson (U.S. Patent No. 5,730,933).

As to claims 126 and 127, Freistedt et al with Horowitz et al teaches sterilizing protected soft tissues. However, Peterson discloses a method wherein a hard or soft protected tissue (such as bone) is radiation sterilized. It would have been obvious to one of ordinary skill in the art to employ the method of Freistedt et al to sterilize hard tissues as well, since one would have had an expectation of success when applying the method of Freistedt et al to the sterilization of hard tissues.

With respect to claims 134 and 135, Freistedt et al does not teach maintaining the tissue in an inert or vacuum atmosphere during irradiation. However, Peterson discloses doing both during irradiation of the tissue. See col.5, lines 28-35. As the introduction of an inert gas or the removal of air from the environment will reduce the presence of oxygen and thus, the production of damaging free radicals during irradiation, it would have been obvious to do the same in the method of Freistedt et al.

As to claims 150, 152, 153, and 154, Freistedt et al is silent with respect to lyophilizing the tissue before irradiation. Peterson teaches lyophilization of tissue before irradiation as a means by which to reduce the presence of free radicals due to water in the tissue. See col.5, lines 53-67. For this reason, it would have been obvious to lyophilize the tissue of Freistedt et al before irradiation thereof and to remove the water to a desired level.

With respect to claim 151, the combination of Freistedt et al with Peterson teaches lyophilization of the product, but does not teach that the solvent removed is an organic solvent. Horowitz et al, however, teaches that it is known in the art to combine a radiation sterilization step with another sterilization step such as treatment with an organic solvent. See col.7, line 66 to col.8, line 7. Since it would have been obvious to first treat the product with a solvent to inactivate viruses, it would have been further obvious to remove the solvent before irradiation.

4. Claim 136 is rejected under 35 U.S.C. 103(a) as being unpatentable over Freistedt et al in view of Horowitz et al as applied to claim 125 above, and further in view of Chanderkar et al ("The Involvement of Aromatic Amino Acids in Biological Activity of Bovine Fibrinogen as Assessed by Gamma-Irradiation").

The combination of Freistedt et al with Peterson fails to disclose a rate at which to apply the gamma radiation. Chanderkar et al teaches sterilization of fibrinogen in lyophilized form in the presence of an electron scavenger (potassium iodide). The preparation is irradiated by gamma radiation with a dose rate of 12,500 R/min (7.5 kGy/hr). See pages 283-284. As the conditions and biological material are similar to those of Peterson and Freistedt et al, it would have been obvious to use the irradiation rate of Chanderkar et al in the method of Peterson or Freistedt et al with Peterson.

5. Claim 165 is rejected under 35 U.S.C. 103(a) as being unpatentable over Freistedt et al in view of Horowitz et al as applied to claim 125 above, and further in view of Okrongly (U.S. Patent No. 5,283,034).

The combination *supra* fails to teach packaging the article before sterilization. Okrongly teaches the known packaging of an article to be sterilized by radiation. See

Art Unit: 1744

col.5, line 60 to col.6, line 2. The packaging prevents the recontamination of the surface after sterilization. A step of packaging followed by terminal sterilization is well-known in the sterilization art and would have been obvious in the method of Friestedt.

Allowable Subject Matter

6. Claim 156 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

7. Claim 107 is allowed.

8. The following is a statement of reasons for the indication of allowable subject matter: the prior art of record fails to teach or suggest: the use of a compound effective to increase penetration of the stabilizer or an assay for determining the optimal conditions for sterilizing a collagen containing tissue wherein the turbidity of the collagen is determined and the tissue is repeatedly irradiated until the turbidity reaches a predetermined acceptable level.

Response to Arguments

9. Applicant's arguments filed 25 February 2005 have been fully considered but they are not persuasive.

10. Applicant argues on page 8 of the Response that there "is no teaching that that the use of additional polyols would provide greater tissue protection. In fact, Freistedt teaches away from the use of multiple polyols by describing, as a preferred composition, propylene glycol as a single radio-protectant." The Examiner respectfully disagrees with

Art Unit: 1744

Applicant's assertions. While the Examiner does agree that there is no explicit teaching that the use of additional polyols would provide greater tissue protection, the use of at least two polyols in combination is disclosed by both Freisted et al and Horowitz et al. The addition of a third is not considered to be patentable where the results are not unexpected. Moreover, Freistedt et al is not limited to a single embodiment and clearly teaches that at least two polyols may be used in combination where desired.

11. Applicant's arguments with respect to the remainder of the claims have been considered but are moot in view of the new ground(s) of rejection.


Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh McKane whose telephone number is 571-272-1275. The examiner can normally be reached on Monday-Wednesday (7:15 am-4:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Kim can be reached on 571-272-1142. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1744

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Leigh McKane
Primary Examiner
Art Unit 1744

elm
31 May 2005